

Putnam (Gas. J.)

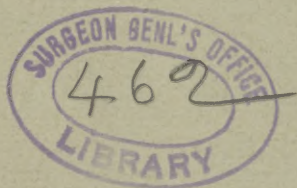
*A Group of Cases of ~~Symptom~~ Scleroses
of the Spinal Cord, Associated with
Diffuse Collateral Degeneration;
Occurring in Enfeebled Persons
Past Middle Life, and Es-
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Studied with Particular Reference to
Etiology.*

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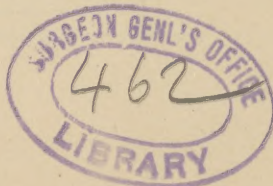
By JAMES J. PUTNAM, M.D., OF BOSTON.

WITHIN the past few years I have seen eight fatal cases for which the diagnosis indicated in the title of this paper seemed to be justified, besides a number of others, of apparently similar kind, which are still in progress or have passed out of my observation. Two cases recently seen, and belonging in this same category, seemed to have been due, in part, to the recent epidemic of influenza. In four instances I have been able to obtain post-mortem examinations, and the conditions of the spinal cords is indicated in the plates that accompany this paper, which were drawn with the camera lucida by Dr. C. D. Young of Rochester, N. Y.

These cases were not all of just the same clinical type, but they present enough points of likeness to lead me to believe that the pathological conditions above noted are of more common occurrence than is usually believed.

The symptoms consisted, in general, of a sub-chronic, progressive impairment of both the sensory and the motor functions of all four extremities, associated after a time

¹ Read in abstract at the Annual Meeting of the American Neurological Association, 1890.



with a moderate and nearly uniform degree of diffuse wasting of the muscles, and, usually, more or less general emaciation. The fatal cases ran their course in about two—in one case four—years, and presented complete paraplegia as a pre-terminal symptom. Possibly the sclerotic changes actually antedated the symptoms, but remained for a time latent, as often happens in disorders of this class.

In three of the cases marked incoördination of movement was present, while in the rest this symptom was absent or inconspicuous. Lancinating pains were present in only one case, and in that one the motor symptoms were spastic far more than ataxic in character.

Of the eight fatal cases, all the patients but two were women; all somewhat past middle life; and almost all were, from first to last, in a condition of considerable debility. In several of them obstinate diarrhœa was a prominent symptom.

Finally, several of the patients, besides being feeble and past middle life, or both, had carried in their tissues, for a long time, small quantities of lead,¹ as proved by urine analyses; and two of them had had malaria. Neuropathic inheritance was present in some of the cases; two of the cords were abnormal in shape or structure, and two, at least, were smaller than usual.

Anatomically, morbid changes were found, to a greater or less degree, in both the motor and sensory areas of the spinal cord throughout its entire length. The medulla oblongata and pons were examined microscopically in one case and found free from material change. The sections from this part did not stain well, but it can, at least, be confidently asserted that the gross changes observed throughout the spinal cord were not present there.

In all the cases, two sets of changes in the cord are recognizable, one of older date, consisting in a relatively dense sclerosis in the posterior columns and in the lateral column (mainly confined to the pyramid tracts); and one of sub-acute character, and evidently of quite recent occurrence. This sub-acute process was, as regards the white columns,

¹ In an analogous case, now under observation, arsenic has been found in the urine in three analyses, covering a period of about two years.

partly in new tracts, partly around the borders of the more dense sclerosis, and was chiefly characterized by the perforated appearance, now familiar to every pathologist, which actually results, perhaps, from the post-mortem changes induced by hardening, but indicates a somewhat rapid destruction of nerve-tubes, with œdematous distention or destruction of the intervening septa, associated with the formation of granule cells.

In the gray horns, the degenerative change (partly recent, partly of older date) was indicated by a disintegration of nerve-cells. In certain parts of some of the cords, indeed, the almost entire destruction of nerve-cells shows that, in them, the ganglionic matter as well as the white columns had borne its full share of the brunt of the degenerative process.

To characterize still further the nature of the morbid process, it may be said that marks of acute inflammation were for the most part absent, though certain qualifications of this statement will be noted later. Even in that one of the cords where, as a cause of the terminal paraplegia, an acute softening seemed to have occurred, so that the topographical arrangement of the white and gray matter of the cord in the upper dorsal region had been almost entirely lost in a general disintegration of the structure, the absence of the signs of cell-proliferation indicated a rapid process of degeneration rather than a typical inflammation. The diseased areas in the white columns were, to be sure, crowded with granule cells, but this condition, though formerly considered as indicating inflammation, is now known to be secondary to a rapid disintegration of myeline, and impairment of circulation, and, in fact, to attend, in some degree, the processes of normal nutrition.²

It is of interest to note that the complete or nearly complete paraplegia which was present in these cases was not, except in one instance, due to any high degree of acute transverse softening in the dorsal region.

It is difficult in Case III. to see why the paraplegia occurred, the changes in the motor tracts are so slight. This

²Simon: *Arch. für Psych.*, etc., Vol. V.

lack of correspondence between symptoms of paralysis and the pathological appearances has, however, been repeatedly commented on.³

No doubt the physiological conditions of circulation in the dorsal cord, which renders it so liable to anæmia (Moxon ; Adamkiewicz) and œdema is largely responsible for the result.

More or less thickening of the pia mater, with cell-proliferation, was noticeable in three at least of the cords, but it was slight and uniform, and not associated with more than a very narrow zone of sclerosis.

Changes in the peripheral nerves were found in one case and may be suspected to have been present in the others, since the nerve-roots were more or less diseased.

The same may be said of the intervertebral ganglia, which were examined in one case.

The histories of the four fatal cases with autopsy are, briefly, as follows :

CASE I. is that of a woman 58 years of age, but appearing much older. Her mother had a tremor (probably senile) for some years before her death ; and her grandfather is said to have become paralyzed somewhat after the manner of the patient herself.

The patient had three children, two of them sons, and in good health, while the third, a daughter, had Pott's disease, and was dwarfed, but intelligent. The patient had had a troubled life, and may have contracted syphilis from a dissolute husband, though the only sign of it was a temporary loss of hair when she was 27 years old.

For six years she had suffered from exhausting and long-continued attacks of diarrhœa, which followed her to the last. Three years before her death her skin began to darken in the normally pigmented areas, and, finally, all over, so that when I saw her, which was in consultation with Dr. M. A. Morris, of Charlestown,⁴ her areolæ were almost black, while the rest of the skin varied from a light brown to a dark chocolate, except that her face and lips were pale, her diarrhœa

³ See Strümpell : *Arch. für Psych.*, etc., XVII., 226.

⁴ To whom for his many courtesies I desire to express my sincere thanks.

having reduced her strength and made her excessively anæmic. The face was covered with epidermal scales and exudation. In temperament she was irritable, eccentric, and wanting in self-control, and showed an indifference and unreasonableness mixed with cunning which, together with the fact that, five months before her death, she had, after great exhaustion, a group of attacks which seem to have been epileptiform in character, suggested cerebral degeneration.

Three years before her death she began to have paræsthesia of the fingers, associated, after a time, with slight incoördination. This condition gradually increased, but did not, for a long time at any rate, involve the legs.⁵ Six months before her death her gait became rapidly, and even suddenly, feeble and ataxic, while the incoördination of the hands also increased, both symptoms being exaggerated by closure of the eyes.

She had no lancinating pains at any time.

At the time I saw her, the pupils were found normal. The cutaneous sensibility of the arms and legs was greatly impaired, but the knee-jerk was exaggerated and ankle clonus was present. The whole body was greatly emaciated, and the muscles everywhere wasted, but not one group more than another.

She exhibited, as she had for a long time, a ravenous appetite for certain articles of food, especially coffee, and a perversion of taste.

Her spinal symptoms increased slowly, but steadily, until in a few months she became paraplegic. The limbs finally became œdematous, bed-sores developed on the sacrum, and she died from exhaustion, without having shown bulbar symptoms. Some degree of sensibility to pricking remained even when the paraplegia was practically complete.

The autopsy was made by Prof. R. H. Fitz, who kindly allows me to use his notes, from which I make the following extracts:

In the lower part of the ileum there were the scars of three ulcers apparently of tubercular origin, though no signs of tubercle were found elsewhere.

⁵ Her mental condition was too unreliable to permit of a satisfactory investigation.

The supra-renal capsules were normal, and all the other organs likewise, except for universal and excessive anæmia.

The cord and one ulnar nerve were placed in Müller's fluid for further examination, but the nerve was afterward mislaid and lost. The brain could not be obtained.

The cord was completely softened for about an inch at the level of the fourth dorsal nerve, but the softening was plainly anæmic in origin, for the cross section, here as elsewhere, showed the tissues, both white and gray, to be absolutely pale, without a trace of color.

The examination of the hardened spinal cord revealed the following conditions:

1. A sclerosis of a portion of the posterior columns and parts of the lateral pyramid tract throughout their whole length, and of the column of Türck, in the cervical region.

2. A recent degeneration of the direct cerebellar tract, beginning at the middle or lower part of the cervical enlargement and stretching upward as far as my preparations extend [upper cervical]; also a similar degeneration, partly older and partly recent, irregularly distributed along the sides of a thickened septum in the anterior root-zone on one side only (Gowers' tract?). The character of this recent degeneration was that already described in the early part of the paper. The glia spaces were enlarged and confluent, giving to the section a perforated appearance, the openings containing the remains of nerve elements, staining faintly with Weigert's hæmatoxylin, and the remains of granule cells.

In the other cords of this series cells of the glia were distinctly swelled, but in these specimens that was not especially noticeable.

This recent, subacute process is probably due to œdema, such as characterizes the obstruction of lymph vessels and the first stage of myelitis. It has often been described, and of late has been studied by Schmaus.⁶

This same appearance of acute degeneration or œdema is met with along the borders of the older and more dense sclerosis in the lateral columns and the posterior columns.

⁶ Schmaus' *Die Kompressions-Myelitis*, etc. Wiesbaden, 1890.

The position of the sclerosis in the posterior columns is as follows: In the upper cervical levels the entire space between the posterior horns is involved, with the exception of a narrow layer adjoining the gray matter and the commissure. (See Plate I., A, B. In most of the sections at the level of A the unaffected area is narrower than here indicated.)



CASE I. UPPER CERVICAL. A.

It will be seen that the area of the lateral pyramid tracts are only partially and unsymmetrically sclerosed, being separated from the direct cerebellar tract by a layer of relatively healthy fibres.

The limiting layer of unaffected fibres in the posterior columns should have been drawn narrower, as in the next section.

Scattered fibres in the sclerosed columns of Goll are unaffected, which lower down appear as definite tracts.

In passing downward toward the lumbar enlargement, there is a gradual tendency to the withdrawal of the more dense sclerosis into two broad bands, lying partly in the column of Goll and partly in the column of Burdach, and diverging toward the dorsal surface of the cord (Plate I., C), and a median strip lying mainly ventral of the areas

just described. Through a portion of the cervical enlargement, the inverted V-shaped area indicated in Plate I., B, is also free. The "posterior outer" field of Strümpell, or column of Bechterew, is involved by a recent degeneration analogous to that in the cerebellar tracts, at all levels of the cord to a greater or less extent, sometimes very seriously. This change is not indicated on the plates; but it is important, because rather characteristic of the "combined" sclerosis as contrasted with locomotor ataxia (Strümpell).



I. MIDDLE CERVICAL B.

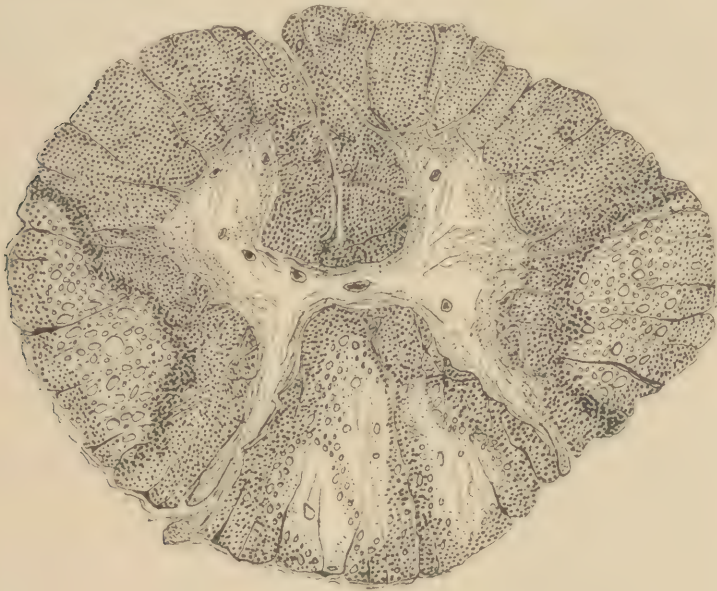
Note the irregular and incomplete sclerosis in anterior and lateral pyramid tract. The "recent degeneration" bordering on the old is indicated by circles (see text). The degeneration of the direct cerebellar tract is, however, recent, though not so indicated.

The lateral pyramid tract was more or less affected throughout its length, though less severely than the posterior columns, but whereas at the middle and lower levels⁷ the sclerosis occupied nearly the whole of the tract, and in the cervical region it occurred more diffusely, in patches, leaving parts of the tract free.

⁷ I could not obtain the greater part of the lumbar enlargement for examination.

The nerve-roots were everywhere more or less diseased, the anterior somewhat more so than the posterior, yet all contained a large proportion of healthy fibres, the number varying at different levels of the cord and for different parts of the root.

On the whole, the relative integrity of the posterior nerve-roots and root-zones caused the Weigert stained sections to present striking contrasts. The changes in the roots were partly recent, partly old and associated with hypertrophy of the connective tissue.



I. UPPER LUMBAR. C.

The lateral sclerosis is, in the deeper parts, more dense than here indicated.

It is especially noteworthy that the degeneration in the anterior pyramid tract was present in marked degree only through a limited portion of the cervical enlargement (Fig. I.), and even here it showed itself only in patches. Throughout the whole length of the cord, however, even to the upper lumbar levels, a few degenerative spots of recent date were to be found in this area.

In the upper dorsal region occurred the transverse destructive process which had caused the complete paraplegia. Of this I will only say that the signs of active inflammation were conspicuously absent. The destruction of the columns of Clarke at this level may have been concerned in causing the degeneration in the direct cerebellar tract above; but this is not to be seen in the lower sections from the cervical enlargement, though it is complete at or below the middle of the enlargement.

The gray matter throughout the length of the cord was the seat of more or less serious degenerative changes.

The nerve-cells were few in number, and while some of them were nearly normal in appearance, almost all had undergone more or less change. Their processes were to be followed but a short distance; and they themselves were coarsely granular, and often without nucleolus or nucleus, and shrunken in volume.

It was difficult to say that any special group of cells had preëminently suffered. In some sections only a very few cells were to be seen, either in the anterior lateral or posterior horns.

The columns of Clarke below the softened portion seemed on the whole to have suffered less than the rest of the gray matter, but were not free from disease. The cells were reduced in number, and the fibres which traverse the area were less conspicuous than usual. (Lissauer.)

The same was true of the fibres of the posterior commissure, and perhaps also of the anterior.

The larger blood-vessels of the gray matter of the septa were sometimes empty and shrunken together, sometimes distended, and their sheaths contained a moderate number of leucocytes.

The Lissauer fine fibre tract near the apex of the posterior horn, though perhaps damaged, was not systematically involved.

It is not my intention to discuss at any length the topographical arrangement of the sclerosis in these cases, but I will simply refer to two papers, by Popoff and by Fran-

cotte,* in which attention is called to the fact that the column of Goll is really divisible into an outer and an inner portion, which develop at different periods, and may degenerate independently. Indications of this arrangement are seen in many of the sections taken from these cases. Finally, distinct degenerative changes of diffuse character, and apparently recent, were found in one or two of the cervical intervertebral ganglia.

CASE II.—The next two cases I saw but once, in consultation, and for the notes of the essential points in their histories on which alone I shall attempt to report, I am indebted to their attending physicians, Dr. A. N. Blodgett and Dr. M. A. Morris respectively.

The first of these cases is that of a woman of sixty, of active and energetic temperament, who is said to have been in good health until within two or three years before her death, that being the duration of her spinal symptoms. There was no reason to suspect syphilis.

The first symptom that greatly attracted her attention was a prolonged attack of diarrhoea which left her prostrated.

From this time on she was unable to go about as before, and suffered greatly from a sense of "numbness" in the feet, and from pains in the back and legs, which were at times of a lancinating character. On closer examination it was admitted that these symptoms were present in some degree for some time before the attack of diarrhoea, but they certainly grew rapidly worse after it. She very soon found herself unable to walk in the dark, and not without staggering even in the light. The general sensibility in the feet was found diminished, and, simultaneously, a slight degree of ankle-clonus was found to be present, and the knee-jerk exaggerated. A progressive tendency to contracture next showed itself.

By the end of a year similar symptoms had involved the hands and arms, and had progressed in the legs so far that walking was practically impossible.

* Arch. Neurol., March and May, 1890.

The loss of sense of position was noticeable in a high degree, and the cutaneous sensibility was greatly impaired, especially below the knees. The general feebleness increased, and the limbs became œdematous three or four months before her death. The pains continued, and the contractures became so great that the knees were drawn almost to the chin and pressed together, while the arms were affected to some degree in the same manner. There was general and excessive emaciation and wide-spread muscular wasting of diffuse character.

For some weeks before her death the urine was passed involuntarily. The mental condition was pretty good until the last month or so, except that she had become nervous and anxious.

Toward the last she lost flesh rapidly and had mild delirium. At intervals she cried out as if from pain, but most of the time was quiet.

Death occurred quietly and apparently from exhaustion, without new symptoms.

The autopsy was made by Dr. A. N. Blodgett and myself. The body was greatly emaciated, and the arms and legs still retained nearly the position given them by the long-standing contracture. There were several small excoriations on the legs, due to pressure and rubbing against one another, and the skin over the sacrum was of dark color, but not ulcerated.

The dependent parts of the body were œdematous. The organs were all very pale, but to all appearance healthy. The heart was empty and remarkably small, even for a woman.

The brain was removed, and appeared to be perfectly healthy, except for a moderate amount of atrophy of the convolutions. It was not examined microscopically.

The pons and medulla were examined, but did not stain well, and I cannot positively assert that they were wholly free from disease, though no marked changes could be detected.

The examination of the spinal cord gave the following results :

1. Sections made while the cord was still fresh showed extensive granule-cell formation (*Körnchenzellen-Myelitis*), which was especially marked in the neighborhood of the sclerotic areas.

2. Sections made from the hardened specimens showed a dense sclerosis—

(a) Of the lateral pyramid tracts.

(b) Of the columns of Goll.



CASE II. UPPER CERVICAL.

The clear space in the centre of the drawing indicates an accidental tear in the preparation, due to post mortem softening.

In the sections from the lower dorsal levels upward, the direct cerebellar tract, and, to a moderate extent, the parts adjoining this and also those adjoining the lateral pyramid tracts, were found involved; but the process here

was evidently of relatively recent date, and the line of demarcation between the two tracts was strongly marked.

The anterior pyramid tract was not involved, or only showed, here and there, traces of recent partial degeneration, giving rise to the perforated appearance already alluded to.

The more dense and older sclerosis of the posterior columns was most extensive in the cervical and upper dorsal regions, where it encroached somewhat on the columns of Burdach, while in the lumbar enlargement it



CASE II.

A short distance below preceding section. Posterior horns displaced in both cases. At the apex of the sclerosed areas is a column of relatively unaffected fibres.

had drawn together into two oval areas, occupying the middle of the column of Goll on each side.

The tract of Bechterew ("posterior outer" field of Strümpell) was nearly free from disease. The Lissauer tract was but little affected at the point of the posterior horn; but, nevertheless, throughout the posterior cornu there were indications of a degenerative change of recent date, apparently involving systems of fibres running at an

angle with the transverse sections, and also the nerve-cells of the cornu.

The lateral limiting layer was intact, except for indications of slight, recent tissue-change—perhaps due to ante-mortem œdema, perhaps to post-mortem influences.

The nerve-roots were far less affected than the long spinal tracts, though they contained many altered fibres or their remains. The posterior roots were less involved than the anterior.

The ganglion-cells of the gray matter were affected somewhat at all levels and in all the groups, but were nowhere completely destroyed.



CASE II. DORSAL.

Considerable areas of diffuse degeneration of slight degree; indicated by lighter shading.

The cells of the columns of Clarke were seriously degenerated, and the changes here as well as in the rest of the gray matter were more pronounced in the lower portions of the cord than in the upper portions.

The pia-mater, especially in the lower dorsal and lumbar

regions, was thickened and adherent, and contained large numbers of nuclei, which also thickly studded the walls of the blood-vessels. Border sclerosis was present to a slight degree, as indicated by the grayish zone on dorsal, Fig. II.

The muscular atrophy, though in the end amounting to extreme emaciation, was never sharply localized, and this would seem to indicate that the degeneration of the ganglion cells, though very likely primary, had not the malignant character of that seen in typical amyotrophic lateral sclerosis and progressive spinal amyotrophy, if indeed it was the main cause of wasting.



CASE II. UPPER LUMBAR.

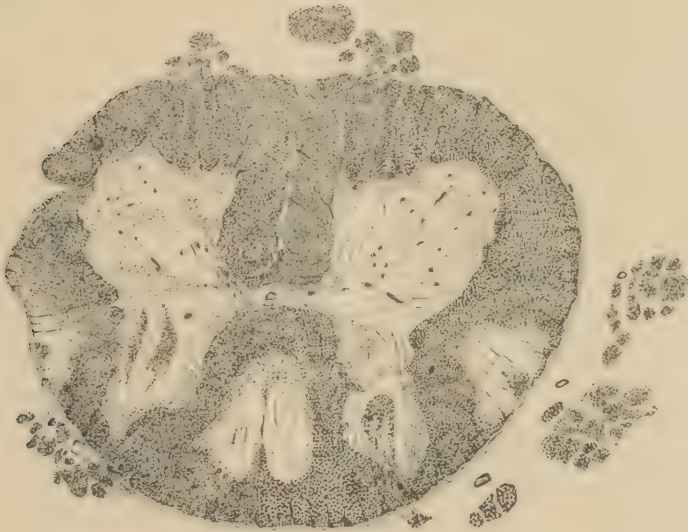
As regards the position of this case among the "combined sclerosis", it is to be noted that it presents a mixture of sensory, ataxic, spastic, and amyotrophic symptoms, and I would call attention here to the justice of Dana's⁹ criticism of Strümpell's¹⁰ familiar classification of the "primary sclerosis."

⁹ N. Y. Med. Record. 1886.

¹⁰ Arch. für Psych., Vol. XVII.

that it does not do sufficient justice to the claim to a separate position, of a group of cases differing widely from locomotor ataxia in their clinical history, yet differing equally or still more widely from spastic paraplegia, in that ataxia is a prominent symptom.

It is certainly true, if appearances may be trusted, that, as in some of Westphal's¹¹ cases, the posterior sclerosis in all my cases, was older than the lateral sclerosis. Strümpell would class such cases as belonging to the general category of "tabes," but the propriety of this I cannot see, and



CASE II. LOWEST LUMBAR.

Symmetrical wedges of unaffected fibres occupy the mid-periphery of the lateral tracts.

the simple fact that my group of patients were almost all women would militate strongly against the admission of the diagnosis of locomotor ataxia. More probable is the general view that besides the influences which produce the typical sclerosis of Strümpell, etc., there are others [v. etiology] which may eventually cause sclerosis of all the tracts, but which act most strongly on the posterior columns.

¹¹ Arch. für Psych., Vol. IX.

It is possible that the relatively recent degeneration in the direct cerebellar tract may have been secondary to a disease of the columns of Clarke, but though this disease is obvious it is not complete, and in fact no greater than that which has occurred throughout the rest of the ganglionic matter of the cord, and this was not sufficient to cause any such change in the tributary anterior nerve-roots as is to be observed in the direct cerebellar tract.

It would be interesting to pursue the topographical analysis further, in the light of the observations of Lissauer, on the fine-fibre tracts of the posterior horns and the recent secondary degeneration experiments of Tooth,¹² which indicate different sources and functions for the fine and large fibre systems of the direct cerebellar tracts, but the state of the sections and my experience with normal specimens do not warrant the attempt. Certain of these points will be referred to later.

An important feature of the sections consists in the fact that they show a curious distortion of shape of the cord in the cervical region, suggesting the possibility of a certain degree of abnormality of development which may have given the underlying tendency to the degenerative disease.

At the upper end of the deformed portion, the posterior fissure forms a deep notch, and the notch at the opening of the anterior fissure is also somewhat deeper than usual.

A little lower down, the posterior or dorsal notch expands into a deep bay, which extends inward in a somewhat lateral direction, leaving, as its outer boundary, a broad tongue of sclerosed tissue, with a small area of relatively healthy tissue at its tip.¹³ It is difficult to conceive how this change of shape should be explained on the exclusive principle of shrinkage, either ante-mortem or during hardening, especially as no such appearance is seen in any other part of the cord. The amount of gray matter in the cervical cord was, also, less than usual.

The walls of the blood-vessels were in general somewhat

¹² Secondary Degenerations of the Spinal Cord : London, 1890.

¹³ This recalls the small area in the column of Goll usually found unaffected in Tooth's experiments (l. c.).

thickened, but this change was not so marked as in Case IV.

CASE III.—This patient, who was seen in consultation with Dr. Morris of Charlestown, was a woman of 51 years, married but without children. Her father died at 64 years; her mother at 60 years, both with what was called "consumption of the blood." So far as could be learned, she had never had syphilis. Three sisters were living and well.

The patient had been well herself up to nine months before her death, except that she was extremely anæmic and delicate, and of an unusually gentle and quiet disposition. She then began to suffer from dyspeptic symptoms of general character, but persistent. Four months later she felt a numbness in her hands, attended by more or less weakness, and incoördination, so that writing became impossible.

About two months later she began to have pain in the left leg, along the course of the femoral vessels, attended by swelling of the whole leg.

This improved somewhat after a time, but was soon followed by swelling of the right leg about the ankle, and by numbness of both legs, incoördination, and loss of power; also by marked loss of cutaneous sensibility.

These symptoms gradually increased, and gave place, shortly before her death to complete paraplegia of the legs. There were no mental symptoms.

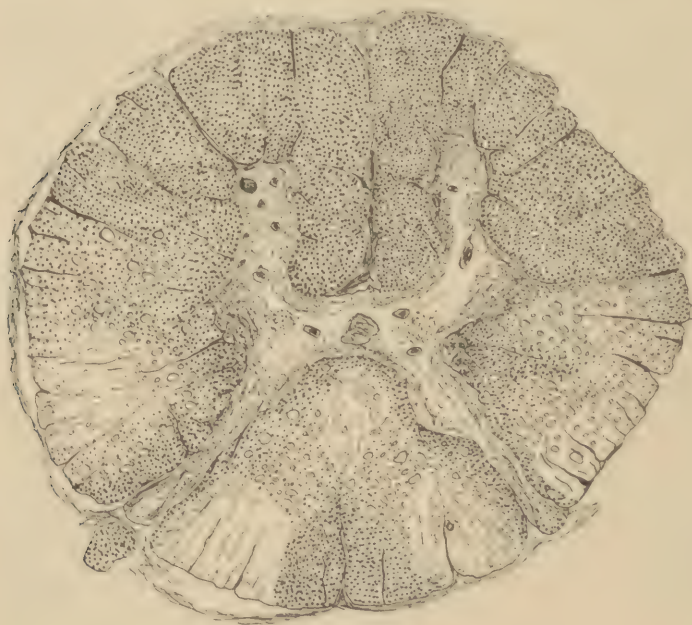
The autopsy was made by Dr. W. F. Whitney, of Harvard Medical College; the subsequent examination of the central nervous system by myself.

The thoracic and abdominal organs presented no morbid appearances of importance, except those of anæmia. The brain and cord appeared very small, though the patient was a small woman. The brain was perfect in form, the membranes were not diseased nor adherent; the convolutions were not atrophied. The cord alone was examined microscopically, after being hardened in Müller's fluid.

The sections showed a sclerosis in the posterior columns, and to a less degree in the lateral columns, throughout the whole length of the cord. (Figs. Case III.) The central and dorsal portions of the columns of Goll were relatively unaffected at all levels, but the "posterior outer" area of

Strümpell and Bechterew was everywhere invaded, either by the older or the more recent changes. The greater part of the fibres of the posterior roots were normal in appearance, but there were more diseased fibres than in the anterior roots. The posterior root-zone and the layer of the fibres along the posterior cornu were, for the most part, unchanged.

The gray matter was less affected than in any of the other cords, though not free from disease. Of the cell groups, the anterior inner group showed the greatest reduction in cells relatively, and the greatest number of shrunken cells. Some of the cervical sections showed a spot of disintegrated tissue near the middle of the anterior horn.



CASE III. DORSAL.

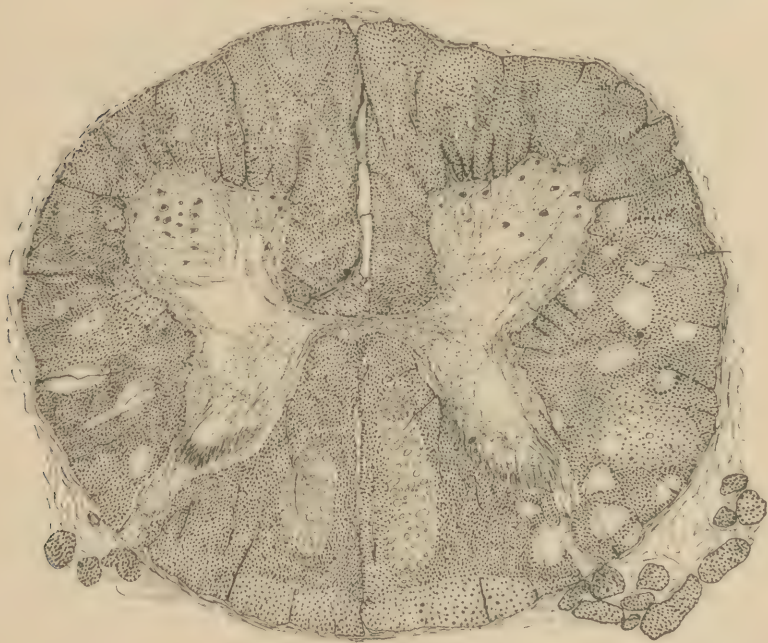
Sclerosis of "posterior outer field" (Strümpell ; Bechterew) ; diffuse and apparently recent degeneration in lateral tracts ; enlarged vessels in gray matter.

The cells of the columns of Clarke, and perhaps those of the anterior horn as well, were of unusually small size, corresponding to the small size of the cord. The fine fibre column of Lissauer seemed to be distinctly diseased, but the

staining was perhaps not perfect enough to decide this point. Many fine points were visible in this area, but they appeared, on close examination, to be the cut ends of connective tissue fibres, which were very conspicuous.

The changes in the lateral columns were rather diffuse, and not exactly coextensive with the pyramid tracts. The cerebellar tract was unaffected. The pia mater was somewhat thickened, and here, as well as in the posterior roots and in various parts of the cord, numerous large (relatively to the other cells) ovoid cells, perhaps of endothelial character, were to be seen.

The other most striking features were: (*a*) the great number of the cells and nuclei of the glia, some of them at



III. LUMBAR.

The sclerosis in the central portions of the columns of Goll is more strongly marked than here indicated; and the contrasts in the lateral columns are not so definite.

points of intersection, surrounded by considerable protoplasm (œdematous?); others long and slender and lying

in large numbers parallel with the fibres, so as not to be seen in their length except on longitudinal sections ; (*b*) a distortion in shape of the anterior horns (not shown in the figure) at a part of the upper dorsal region. Instead of lying parallel, the two horns diverge widely, so that their inner edges look almost ventrad. This is a recognized anomaly, and its presence, associated with other peculiarities that have been mentioned,¹⁴ suggest an imperfect development that may have been one of the underlying causes of the disease ; (*c*) the remarkably large size of the vessels, not only the fine arteries of the sclerotic area, but, to an even greater degree, the larger vessels of the gray matter. Besides being of great size, as if dilated, the walls of all these vessels were thickened and hyaline, and many of them were surrounded by leucocytes.

I do not know to what to attribute this condition, nor to what extent it may have contributed to the degenerative tendency ; but Buzzard¹⁵ has reported a case of locomotor ataxia where a similar vascular dilatation was noted by Bevan Lewis, and this writer, in his recent work on Mental Diseases, makes a disordered vaso-motor action leading to dilatation, of cerebral origin, responsible for the spinal sclerosis in many of the cases when this accompanies parietic dementia. His reasoning does not appear to me fully convincing.

The disease in the motor tract of this cord was so much less than that in either of the others, that it seemed inadequate to explain the terminal paraplegia (see page 3).

CASE IV.—The clinical history of this case has already been published,¹⁶ and I shall refer to it only very briefly, and mainly for the sake of calling attention to its pathological relations. It is especially interesting as being one of the cases where the disease may have been due in part to lead poisoning.

To sum up the clinical history, we have a man in middle life, a carriage painter for many years, living under comfortable

¹⁴ See also below, under Etiology.

¹⁵ Brain, 1888.

¹⁶ Transactions of the Association of American Physicians, 1889.

conditions, suffering for two years with progressive paræsthesia, a moderate degree of anæsthesia, beginning in the hands and feet, and muscular weakness of both arms and legs, without local symptoms, and with but little if any real incoordination. The knee-jerks were exaggerated and ankle-clonus was present.

The electrical irritability of the affected muscles was moderately diminished. We find these symptoms associated with very marked paleness of the skin, of light yellow cast, general emaciation and weakness, and the presence of albumen and casts and lead in the urine. All these symptoms increased slowly, but steadily, and terminated in complete paraplegia, with incontinence of urine, shortly before



CASE IV. CERVICAL.

This and the following drawings are slightly diagrammatic.

The degeneration in the direct cerebellar tract and the greater part of the annular degenerated layer is "recent," as indicated here and there by the circles.

The columns of Goll are wholly affected, but in the outer portion many fibres persist.

death, which occurred about two years after the onset of the first symptoms. His mother is said to have had similar symptoms, associated with diarrhœa and œdema of the feet and ankles, for several years before her death.

Toward the last he showed mild delirium and dizziness,

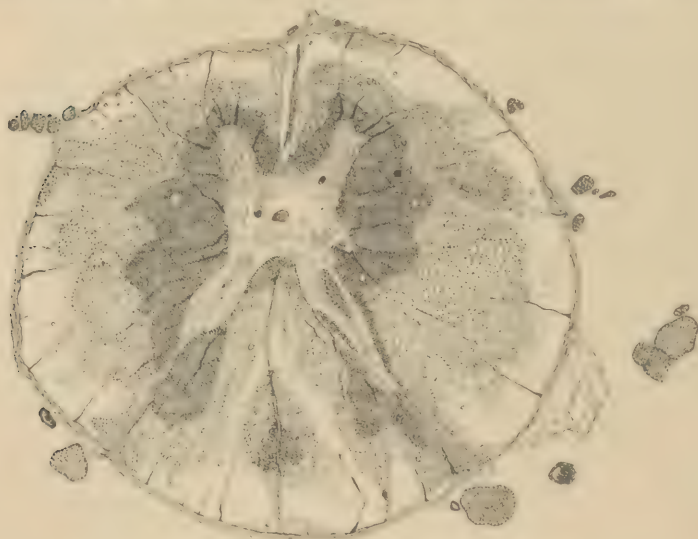
probably due to anæmia or œdema of the brain. There was some swelling of the feet and legs. Death occurred from gradual failure of the heart and respiration.

The autopsy was made by Dr. C. C. Tower, of S. Weymouth, to whom I am indebted for his notes of the case, and for permission to prepare and examine the nervous tissues.

In the fresh state the entire white mantle of the cord was found crowded with granule cells.

The spinal changes in this case (Figs. IV), differed from those already described in the following respects :

1. The thickness of the pia was somewhat greater, and may be suspected to have given rise to a species of annular sclerosis, though not to the degree which the drawings indi-



CASE IV. DORSAL.

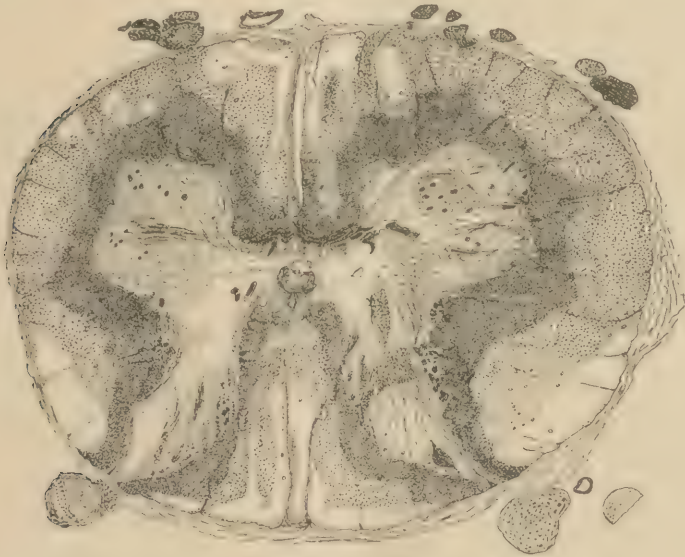
In this and several other drawings of the series (especially Case I.) there are indications of the division of the columns of Goll into outer and inner part (see text, page 11).

cate, the changes in the direct cerebellar tract, for example, being of recent date, and characterized by enlarged glia spaces still containing homogeneous masses staining faintly with carmine and with hæmatoxylin. Meningeal symptoms were conspicuously absent.

2. The sclerosis of the long tracts, and especially of the pyramid tract, was less regular in its distribution, and is more likely to have been caused or increased by secondary degeneration, which, in the case of the posterior columns, may have originated in peripheral neuritis.

3. The nerve-roots, especially the posterior, were much more seriously involved. Sometimes a mass of sclerotic tissue, in a nerve-root, lay side by side with a comparatively normal portion.

4. The columns of Goll contained many scattered axis cylinders, usually of small size, separated from each other by a homogeneous substance staining well with carmine.



CASE IV. LUMBAR.

Supplementary canal beneath the main canal. Varying degrees of degeneration of different roots and different parts of the same root, as indicated by the darker and lighter shading.

All the ganglion cell groups, including the columns of Clarke, had suffered greatly, and in proportion to the general denutrition, which was most marked in the lower dorsal region.

5. The hyaline degeneration of the vessels was much more strongly marked. At the lower dorsal and upper lumbar

levels, the recent process of degeneration or inflammation (œdema) had attained such a degree of activity that many of the parts not yet destroyed, the nerve-roots, especially the posterior, the fibres of the root-zones, the gray matter, the glia tissues, were in a state of active change.

In the carmine sections, the axis cylinders were to be seen in every stage of swelling, vacuolization and destruction.

As strongly against the exclusive meningitic origin of the marginal changes is the fact that it is not present in the lumbar region, except in the anterior columns, though the meningeal thickening is as great there as elsewhere. The drawings are somewhat diagrammatic.

In the dorsal, cervical and lumbar regions little else of the white mantle besides the limiting layer was free from disease, and even that was not wholly untouched.

In spite of the general tendency to degeneration, the Lissauer tract in the lumbar region contains a large number of fine fibres, and the fine fibres of the columns of Clarke are, at some levels, to be well made out, though the cells are largely altered and reduced in number.

The hyaline thickening of the vessels forms, perhaps, a part of a general arterio-fibrosis, to which the urinary signs may have been due. The other usual signs of chronic nephritis were not noted during life. It is also possible that the patient's prolonged exposure to lead may have partly initiated this series of changes, lead having been twice found in his urine.

Examination of fibres teased out in osmic acid from cutaneous and muscular filaments of the anterior crural and peroneal nerves, showed well-marked degeneration of some fibres with persistence of others, the change being far less than would be expected had the whole process been primarily one of neuritis.

Besides the general impaired nutrition, the patient was perhaps under the ban of inherited predisposition (see below under etiology).

The clinical notes of the four other fatal cases will be given in the Appendix.

I wish to speak briefly of this group of cases from the standpoint of pathological diagnosis and relationship; etiology; clinical diagnosis; prognosis.

We have the following pathological conditions to account for:

1. A relatively chronic sclerosis in the posterior and lateral centripetal and centrifugal long tracts.

2. A more acute and recent degenerative change in adjoining areas, partly diffuse and partly systemic in distribution.

3. A diffuse degeneration of varying severity and uncertain duration in the ganglionic matter of the cord, and probably the intervertebral ganglia.

4. Degeneration of moderate degree in the nerve-roots and peripheral nerves.

1. There seems to me no sufficient reason for refusing the name of *primary combined sclerosis* to the first of these conditions, in spite of the somewhat diffuse character of some of the lesions. Of course, the term "primary sclerosis" is to be taken as a provisional expression, and not as indicating the definite adoption of a pathological theory. It is highly probable that the sclerosis of the long tracts sometimes occurs because the cells from which they spring have lost something of their trophic energy,¹⁷ but this is not necessary, and is often only one of the conditions that makes a tract or a nerve vulnerable to other influences.

That a part of the degeneration, for example that of the direct cerebellar tract in Case I., was of the nature of secondary degeneration, is not doubtful, but it would be straining after an unreal pathological simplicity to reject the doctrine of primary degeneration altogether unless the evidence is clearly against it.¹⁸ On the contrary, where there are reasonable grounds for admitting it, we should welcome it as a possible way of obtaining new light on the etiology of these obscure affections.

As regards the recent subacute process of degeneration,

¹⁷ Compare O. Vierordt; Arch. f. Psych., Vol. XIX.; also a discussion on a paper by Hoffmann. Ibid, 1888, p. 710.

¹⁸ See Ballet and Minor, Arch. de neurologie, 1884; Popoff, Ibid., 1885.

in and around the older sclerotic areas, in new tracts, in the nerve-roots, and in the ganglionic matter of the cord and the ganglia, it will be sufficient for the purposes of our present inquiry, as to the probable etiology of the main disease, if we admit the suggestion that in so far as this was not due to secondary degeneration, or to the local impairment of nutrition, it may indicate a general enfeeblement of nutrition and circulation of the whole body, and bear out the view that the same influence may have contributed to develop the primary disease.

The nerve-roots were more or less altered in all the four cases; and in Case IV. some of the muscular and cutaneous branches of the anterior tibial nerve were found (osmic acid) to contain both diseased and healthy fibres. I know no way of telling whether these changes were secondary or primary, from the histological examination alone.

Such evidence as points to peripheral neuritis, as a part of the primary process, will be given under *clinical diagnosis*.

Finally, it is probable that a part of the changes in the gray matter were primary, and of the same date, and even the same origin with the sclerosis of the long tracts.

CLINICAL DIAGNOSIS.

Most of what needs to be said under this head has been already noted.

Supposing the "combined sclerosis" to have been the primary lesion in these cases, it remains to be considered in what relation they stand to other groups of cases of similar pathology.

Strümpell, who has discussed this subject in a series of careful papers,¹⁹ recognizes four varieties of primary sclerosis: 1, the "family form" of locomotor ataxia, known as Friedreich's disease; 2, the typical locomotor ataxia; 3, the spastic form of tabes (in which the lateral columns are believed to be primarily and mainly affected; the posterior columns later and less); 4, intermediate forms between the last two.

¹⁹ Arch. f. Psych., etc., Vol. XVII.; also Vols. X., XI.

Dr. C. L. Dana, of New York, in his paper upon the same subject, published in the "N. Y. Medical Record" for 1886, justly criticises this classification as not adequately recognizing that form in which ataxia is prominent, and the posterior columns principally affected, and yet which presents a clinical history quite different from that of locomotor ataxia.

In most of the cases reported in this paper, the pathological or clinical signs indicated a greater disease of the posterior than of the lateral columns. Yet neither their course nor the symptoms were characteristic of locomotor ataxia, and most of the patients were women and non-syphilitic, and thus doubly unlikely to have locomotor ataxia.

The difference between these different types seems to me, however, hardly more striking than the signs of relationship between them, as shown by similarity of etiology, the frequency of mixed forms (Strümpell's fourth group), the transition of a simple into a combined sclerosis, the frequent involvement, early or late, of the ganglionic matter in the degenerative change.

In this connection I would call to mind the varieties of spinal degeneration met with in connection with chronic paralytic dementia. These forms include the posterior sclerosis, lateral sclerosis, combined posterior and lateral sclerosis, incomplete types of the latter form, multiple sclerosis (Schultze), amyotrophic lateral sclerosis.

The diagnosis of these mixed and irregular types such as I have reported and which I believe to be not infrequent, of course, rests on the recognition of sensory and motor symptoms, together with some sign (such as exaggerated knee-jerk or ankle-clonus, paralysis of sphincters, marked incoördination) that these symptoms are of spinal origin. Where it happens that the symptoms are mainly sensory, consisting in paræsthesia of various kinds, associated with a moderate amount of motor weakness and some impairment of electrical irritability, and as in Case III. and of the Appendix, I know of no way of excluding the diagnosis of chronic generalized neuritis, and it is not impossible that, as in locomotor ataxia, more or less

neuritis is sometimes present, even at the outset, as it doubtless is in most of the cases before the close (See Appendix, Case III.).

The chief practical interest of these cases lies in the *etiological* problems which they suggest, and in studying them from this point of view it is not necessary to be so strictly precise as to the category in which we place them. For, although the different forms of spinal sclerosis are by no means all alike in their *etiological* relationships, yet they differ less in this respect than in others.

Besides the fact that almost all of the patients in this group of eight or more were women, and that they were all either debilitated or anæmic persons, and several of them prostrated by exhausting disease, it is noticeable that certain marks of developmental weakness were observable in some of them; and finally, that the toxic influence of lead may be suspected of having played a part in three of the eight fatal cases.

In reading over the voluminous literature of the spinal sclerosis, one cannot, I think, fail to be struck with the fact that the causes which play by far the most important part are: a strain of constitutional weakness, such as is pre-eminently seen in Friedreich's disease, both family and sporadic forms; and specific toxic influences, of which syphilis is the chief. It is true that in a vast number of individual cases other causes seem to have been at work, but for purposes of study I believe that it is the wisest to confine ourselves to those which are the most important, in the hope that by widening our conception of these, we shall find that the others come into line with them to a greater or less extent.

As regards the influence of developmental weakness of the spinal cord itself, the evidence hitherto accumulated is small, but it is enough to suggest that abnormality of shape or structure or small size, either predispose to disease, or form a correlated manifestation.²⁰

²⁰ See Art. Rückenmark, by A. Pick, Real-Encyclopedie, second edition. See, also, Strümpell; Arch. für Psych., etc., XVII., 233.

An interesting table indicating the small size of the cord in Friedreich's disease, has been drawn up by Blocq and Marinescu²¹, and I have copied it in a condensed form, in order to compare their figures with those taken from my cases.

Unfortunately, neither the sex nor the size of the patients from which their measurements were derived is stated. The first three of my cases were women, and under rather than over the average size.

BLOCQ AND MARINESCU.			PERSONAL CASES.			
	Normal Cord.	Friedreich's Disease.	Case 1.	Case 2.	Case 3.	Case 4.
Largest cervical section...	14 x 9½	10 x 7	10 x 9	9½ x 8	11½ x 8	13 x 10
Smallest dorsal section	9½ x 7½	5 x 5	6½ x 6½	7½ x 6½	6¾ x 6½	7¾ x 8
Largest lumbar section	10 x 9	8½ x 8		9½ x 8	9 x 8	10 x 9

The significance of anatomical abnormalities is discussed by F. Schultze,²² with reference to congenital fissures and cavities, irregularities in the arrangement of white and gray matter, smallness of cord, imperfect development of myeline, as perhaps occasionally leading to one or another form of disease, though not incompatible with health, especially if the function of the part is not subjected to spinal strain.

Kahler and Pick²³ report an extensive sclerosis of the posterior columns, with very small dorsal cord, diminutive posterior horns, imperfect development of the columns of Clarke, etc.

²¹ Arch. de neurologie. May, 1890.

²² Abstract, in the Arch. f. Psych., etc., Vol. XI., p. 270.

²³ Central Nerven-System, 1879, p. 102.

Buckholz²⁴ reports a combined sclerosis, with abnormal shape of the gray matter.

The abnormalities in Cases II. and III. of those here reported have already been indicated. The sections in Case IV. showed two slight peculiarities not yet described, which are not unworthy of mention. One was a double canal in a part of the lumbar enlargement, no very rare anomaly, but one which I have seen in a case of Friedreich's disease, reported by Dr. S. Everett Smith, with a microscopic examination by myself.²⁵ The other was a deep and narrow indentation running very obliquely into one anterior-lateral column in a portion of the cervical enlargement, so that a broad tongue of nerve tissue lay separated from the rest of the white substance by a mass of loose connective tissue growing inward from the pia mater.

The interest of these peculiarities is increased by the fact that the patient's mother appears to have suffered, in advanced years, from symptoms resembling his.

In regard to the influence of the neuropathic condition in general, as predisposing to sclerosis, it is difficult to form an accurate opinion, since greater or less degrees of this temperament are so common. I believe, however, that among the cases of combined sclerosis, even exclusive of Friedreich's disease, we shall find a larger proportion of neurotic subjects than in other forms of sclerosis. This was true of Case I. in my group. Case IV., and perhaps Case III., though they would have been called perfectly normal persons, were of an unusually, not to say unnaturally, mild and gentle disposition.

Kahler and Pick, in the paper just alluded to, refer to certain observations indicating the propriety of regarding acute poliomyelitis as among the neuropathic stigmata in relation to spinal diseases of development. Case II. of the present group had one daughter, who had suffered from this disease in a very severe form, besides, however, having two healthy children.

²⁴ Arch. f. Psych. etc., XXI., p. 230; also Ibid., Vol. XX., Delirium Acutum, etc. See also Strümpell, Arch. f. Psych., etc., XVII., 233.

²⁵ Boston Med. and Surg. Journ.

It has been noted that the majority of the patients in my group of eight were women. I do not know to what to attribute this, unless it be mere accident, combined, perhaps, with the fact that women are possibly even more liable than men to suffer from the debilitating influences that appear to excite this form of sclerosis.

The next most important set of causes are the toxic influences.

It has been established, beyond a doubt, that syphilis, ergot, and lathyrus are direct causes of spinal sclerosis. It is probable that certain diseases give rise to poisons which act in a similar manner, though not with the same frequency. The latest observations in this direction are those of Lichtheim,²⁶ who has reported cases of pernicious anæmia, which seemed to lead to a rapid degeneration of the spinal cord, especially of the posterior columns. The changes involved both the nerve fibres and the neuroglia, and, from their description, it is obvious that that they correspond closely with the more recent processes of degeneration observed in my cases. Lichtheim further says that these changes are absent in pseudo-leucocythemia and chlorosis, but are found in true leucocythemia, and he regards this as an argument in favor of their toxic origin.

Lichtheim refers also to the observations of Fürstner, who found that the abnormal condition of the blood produced experimentally by centrifugal rotation caused similar changes in the lateral columns and pyramid tracts; also the analogous observations of Minnich on the spinal changes associated with chronic jaundice, and those of Tizzoni on the effects of the extirpation of the supra-renal capsules. Degenerative changes in the posterior columns are also said to have been reported in a case of Addison's disease. It is reasonable to suspect that with this large group of cases those reported in this paper stand in close analogy.

The opinion of various observers is in favor of the view that simple impairment of the nutrition acts as a contributive cause in toxic cases of more obvious kinds; thus it is well

²⁶ Verein f. wissenschaftliche Heilkunde in Königsberg. 28 October 1889. Abstract in Centralblatt f. allg. Path. u. Path. Anat. January, 1890, p. 20.

known that Tuezec, who first reported the ergot sclerosis, and more recently Grünfeld,²⁷ failed to obtain experimentally the changes in the posterior columns among ergot eaters, and Brunton, in commenting on this fact, suggests that the miserable conditions of life of the ergot-eating peasants is an essential condition for the result.

On the other hand it is certain that all these disorders of nutrition may be present in an extreme form without exciting spinal changes, and we have yet to learn just what the noxious influence really is. Even the extremely exhausting dysentery of hot countries, as analyzed by Pugibet,²⁸ though it gives rise to paralysis of various sorts, does not appear to initiate these progressive spinal sclerosis.

Three of my eight patients (as well as the mother of Case IV.) suffered from exhausting diarrhoeas through a long period, and one of them had been prostrated by chronic rheumatism and malaria. Within the past year I have seen two patients with symptoms apparently referable to the condition which we have been considering, where the grippe seemed to act as a partial cause.

There is one other influence which is believed to at least contribute to spinal changes, both those affecting the gray horns and the sclerosis of the long tracts, namely, over-exertion or stimulation, with which Lichtheim includes the sensory irritations acting on the posterior columns.

If spinal changes are really brought about in this way—and for the motor ganglionic apparatus this seems to be certain—the fact may be utilized to help clear up the much-discussed matter of the origin of the system degenerations.

It has been established, through the experiments of Wedenski²⁹ and H. P. Bowditch,³⁰ that the nerve-fibre is practically inexhaustible. Even the continuous faradization of many hours leaves it as capable of performing its functions as before.

²⁷ Arch. f. Psych., etc., XXI., 618.

²⁸ Rev. de méd. 1888.

²⁹ Centralblatt f. d. med. Wissenschaften, 1884.

³⁰ Jour. of Physiol., 1885; also, Arch. f. Anat. u. Physiol., 1890.

The parts that tire are the muscle and the nerve-cells, and these of course tire rapidly. From this we may infer that if fatigue is capable of inducing sclerosis, it must be by first exhausting the ganglionic matter from which the long spinal tracts spring.

Paralysis occurs occasionally in acute anæmia, and sclerosis,³¹ but it is usually temporary, and it may be guessed that it is due largely to œdema. The results of cutting off the entire blood supply of the spinal cord are well known, through the experiments of Ehrlich and Brieger, Sprouck³² and Singer,³³ to consist in destruction of the anterior horns and of the anterior lateral limiting layer and anterior nerve-roots, leaving the long tracts relatively unaffected, just the reverse of the picture presented by the primary sclerosis. At the same time, it is very doubtful whether we can argue from acute anæmia to chronic anæmia, since in the latter case the influence of œdema is liable to come in, and this, to judge from the results, slight compression of the cord and its membranes (Kahler; Schmaus),³⁴ is especially prone to affect the nutrition of the white fibres. The condition of the circulation in the dorsal portion of the cord (Moxon; Adamkiewicz), favor the occurrences of anæmic softening in that region, and it is evident that in Case I. we have a typical example of this sort, and in the other cases similar but partial results.³⁵

Before leaving the subject of the toxic sclerosis, I desire to call attention to the possible effect of lead and arsenic in this direction. The facts that are at my command are too meagre to make it worth while to discuss their bearing at any length. I will simply say that I have ascertained by experiments, continued through a number of years, that lead and arsenic are frequently to be found in the urine of healthy persons; and also that I have found lead with rather

³¹ See Leyden, Rückenmarkskrankheiten.

³² Arch. de Physiol., etc., 1888.

³³ Sitzungsber. d. Kais. Acad. des Wissenschaften. Wien. 1887.

³⁴ Die Kompressions-Myelitis, etc., Wiesbaden, 1890.

³⁵ See Max Beck, Inaug. Diss. Breslau, 1888; see also, in this connection, Braun; Deutsches Arch. f. Kl. Med., 1888. Marie; Progrès méd., 1884. Duplay; Arch. gén., 1885.

more than the usual frequency in the urine of persons suffering from spastic paraplegia and from the symptoms recorded in this paper.

In a case of spastic paraplegia in a middle-aged lady of delicate health, who is still under observation, arsenic has been found in the urine three times in two years.

These influences also are perhaps only contributive.

The age of the patients will be next considered briefly as a possible etiological factor in the disease. One hears it occasionally said that old age is liable to bring with it scleroses of the cord; but positive evidence of this kind seems to be rather lacking. Leyden discusses the question, but concludes that it is a degeneration of the ganglionic matter, rather than sclerosis of the white columns that comes with age; and Dana³⁶ comes to a similar conclusion. Ribail³⁷ reports a number of cases where the irritation of the calcareous deposits in the membranes of old people has caused sclerosis, but of a purely local character. Demange³⁸ devotes some space to the subject, and concludes that the sclerosis of old people consists in the thickening of the vessels and connective tissue, but differs widely from system sclerosis.

A number of cases are, however, on record which show that moderately advanced age brings at least no immunity from the primary sclerosis. In my cases the age of the patients only comes in as perhaps sufficiently advanced to increase their feebleness.

In most cases, doubtless, more than one, perhaps many etiological factors are at work, but to save, through prophylactic measures, even an occasional patient from this crippling malady is worth a large amount of investigation. No other causes for the sclerosis and degeneration were apparent in these cases of which I have reported the post-mortem examination, beyond those which I have mentioned. All the patients, except the first—who had had a troubled life, and where a suspicion of syphilis was present—had led

³⁶ Annual Meeting of Amer. Neurol. Association, 1890.

³⁷ Neurol. Centralblatt, 1885, p. 178.

³⁸ *Ibid.*, p. 227; also, Rev. de Méd., July, 1885.

substantially quiet and protected lives, and the more weight is therefore to be attached to the constitutional weakness, the feebleness of nutrition, and the possibility of toxic influences. More persons than we realize may be on the border line of disease, and partial causes are often of prime importance.

The apparent importance of the part played by the anæmia and impaired nutrition in these cases suggests a hopeful outlook through the use of careful and thorough treatment by tonics and nutritives.

So far as I have been able to test these measures, the patients' general nutrition has responded in a measure, but the course of the spinal disease has not been materially modified. This may, however, mean only that the treatment was begun too late.

The increasing importance which toxic influences of various sorts are assuming as among the causes of the spinal sclerosis is presumptive evidence that the morbid change is primarily degenerative rather than inflammatory in character; but this argument, likewise, is a theoretical one, and, in fact, when the matter is viewed broadly, the inflammatory and degenerative, focal and sympathetic processes are found to be united by closer bonds than is generally believed, and to occur under similar etiological conditions.⁴⁰

It is probable that much will be learned in the future by following two lines of research; the first being the relative vulnerability of the different cellular fibrous systems; *i.e.*, their relative liability to suffer under influences acting on all parts alike; the second being the study of the analogy between morbid influences, now seeming to be of different kinds. It is possible that many of them will be found to unite under them.

To sum up, once more, the features that make these cases important, they give us evidence of the occurrence among persons, especially women, of advanced age, constitutional feebleness, or impaired nutrition of somewhat irregular types of "combined sclerosis" of the cord, often of

⁴⁰ See Gowers: *Diseases of the Nervous System*; and Grasset: *Maladies nerveuses*.

relatively rapid course and fatal issue, associated with a tendency to subacute diffuse degeneration. Besides the causes indicated above, this condition may be occasionally due, at least in part, to toxic influences of a preventable kind. Finally, in the early stages of some of these cases, it may be impossible to say whether we have to deal with myelitis or multiple neuritis, and, in fact, both conditions are probably often present together. (See Appendix.)

It might be urged, especially in view of the diffuse changes which I have considered as secondary, or terminal, that the sclerosis of the long tracts was really a secondary degeneration, due to focal myelitis, or to meningitis as Ballet and Minor,⁴¹ Popoff,⁴² Dejerine, Obersteimer⁴³ and other writers have assumed even for many of the older cases of similar kind.

It is, however, improper to urge this origin where the focal disease cannot be demonstrated; and, moreover, as against the assumed improbability of the occurrence of "primary" degeneration of fibrous tracts, we have an important mass of new evidence in the discovery that similar degenerations occur in the brain under conditions more or less analogous to those noted in this paper.⁴⁴

APPENDIX.

NOTES ON THE FOUR FATAL CASES WITHOUT AUTOPSY.

The first case is that of a woman in middle life, seen by me several times, many years ago, in the Out-Patient Department of the Massachusetts General Hospital, and later at her home.

⁴¹ Arch. de Neurologie, 1884, 44.

⁴² Ibid., 1888.

⁴³ Anatomie des Central Nervensystems.

⁴⁴ *Meyer*; Allgem. Zeitschr. f. Psych., etc., 1890, 664. *Cramer*; Faserschwund nach Insolation Allgemeine Zeitschr. f. Psych., etc., 1890, 692; also a summary by the same writer in the Centralblatt f. Allgem. Path. u. Path. Anat., 1890, 3. *Jendrassik*; Ueber die Localisation der Tabes Dors. Deutsch. Arch. f. Klin. Med., Bd. 43, 543. *Hensen*; *Schultze*; Allgem. Zeitschr. f. Psych., etc., 1890, 687.

Her first complaint was of "numbness" in all four extremities, beginning at the periphery and spreading in intensity and extension so as to give a sense of intense paræsthesia to the whole limb. This was associated with marked debility and severe and progressive anæmia. At first there was no marked impairment of motion, but after a time the legs became weak and weaker, though they showed no local paralysis or atrophy. Then followed a gradual increase of paralysis, resulting in paraplegia and death. There had been no pain nor acute symptoms at any time. The whole duration was upward of two years. There had been no typical signs of lead-poisoning, but an examination of the urine had shown the presence of "considerable lead."

The second case is that of a lady sixty-four years of age. Her symptoms began in May, 1887, and she died paraplegic in a little more than one year later.

During the summer of 1887—that is, a few months after the onset of the disease, and when her symptoms consisted mainly in a sense of numbness in the fingers and toes—she was seen in Paris by Charcot, who gave her a written opinion to the effect that she was suffering from slight disease of the posterior columns of the cord.

My notes of the case cover almost the entire period of her illness, but may be condensed as follows: The symptoms began with the sensory symptoms above noted. To these were soon superadded progressive incoördination of both upper and lower extremities, diffuse emaciation without localized atrophy, progressive loss of cutaneous and muscular sensibility and impairment of muscular power. The urine was free from lead, and there were no signs of chronic nephritis or mellituria. There was no incontinence of the urine until a short time before her death, when the weakness of the lower extremities increased to complete paraplegia, attended with the formation of bed-sores. No autopsy was permitted. The patient was unmarried, non-syphilitic, and lived under the best of conditions for general nutrition.

The third case is that of a man, about fifty years of age, and latterly a postmaster by profession. He had been in the army, but had never contracted syphilis. He suffered, however, both while there and later for many years after, from chronic diarrhœa, chronic malaria and rheumatism, through which his constitution, previously a fine one, became undermined, so that during the period that he was under my observation he was pale and thin.

The case is also important from the fact that here, as in several other instances, lead was twice found on examination of the urine, though it was not traceable to any special source.

His symptoms consisted in an intense sense of numbness of all four extremities. To speak more exactly, the feeling complained of was as though the limbs were encased in some hard substance and packed in ice. These symptoms were much more strongly developed in the lower than in the upper extremities, as was the case with all my patients. The motor symptoms consisted in a very slowly progressive feebleness, without loss of any particular movement. The knee-jerk was absent, but there was no incoördination. There were no bladder symptoms, unless shortly before his death, when he was no longer under my observation. There was a moderate amount of impairment of cutaneous sensibility, and the electrical reaction of some of the leg muscles was slightly diminished. In general, however, the muscles were fairly firm.

Like one of the fatal cases with autopsy, reported in the earlier part of the paper, this patient improved notably in his general condition and slightly as regards his nervous symptoms under the influence of generous feeding; but the gain disappeared after a time, and he evidently became paraplegic and died in a condition of exhaustion after a few months. Lead was found in the urine.

The fourth case is that of a lady, fifty-one years old, seen in consultation with Dr. C. K. Cutter of Charlestown. The first symptoms had been noticed about two years previously, and consisted in a sense of numbness, referred to the feet

and finger-tips, not at first attended with muscular weakness. Previous to the time of the appearance of these symptoms she had had good health and a good color. Since then she had grown weaker and pale. The weakness of the legs was first noticed six months before my examination, and had increased gradually and steadily, so that she was able to walk but little and could do no work. The sense of numbness had also spread over the whole of the legs, thighs and over the lower part of the trunk, and in the upper extremities it had spread to the elbows. Constriction was felt around the chest and abdomen. For six months or more she had been steadily losing strength and flesh. The skin had also been of a yellowish color, at one period, so that the physician who at that time attended her said that she was jaundiced. She had noticed no special muscular wasting. The sense of constriction was present also in the legs, and at times she felt as if her stockings were filled with pebbles. She had noticed but little, if any, distinct loss of sensibility, yet had observed that a touch on the skin caused a somewhat unnatural sensation. When her legs had lain for some time in the same position she was unable to tell just where they were; but this had not been noticed in regard to the hands.

The patient was pale, with a yellowish cast to the skin, the hair was gray, and she looked much older than her years. She was said to have had a good deal more than the average of intelligence. The sense of touch in the fingers was found perfect for ordinary tests, yet the patient said that the sensation was not quite natural. The sense of touch in the feet and legs was impaired, but slight pressure was felt and pretty well localized. Her gait was uncertain, and there was some static ataxia. The power to distinguish cold and warmth appeared to be unimpaired. A touch with the point of a pin on the feet and legs was at once felt and recognized. The sense of the position of the toes was impaired. The knee-jerk was absent, even with reënfacement. She had had no pains characteristic of locomotor ataxia, and she had no bladder symptoms;

neither was there anything in her history to suggest syphilis.

I never saw this patient again, but learned that she died a few months after my visit, making the duration of the case in all about two years and a half.

Besides these fatal cases, I have seen a number of others, occurring like these in persons past middle life, and presenting similar symptoms.

In one case the urine was found, on three analyses at different periods, to contain lead, and the patient, after having become nearly helpless, finally improved somewhat, so that she could walk about. This case was that of a woman between thirty and forty years of age.

